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Anti-HIV env immunities elicited by nucleic acid vaccines.

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Plasmid DNA vaccines encoding HIV-1 env were used to immunize mice and nonhuman primates. Plasmids were prepared that produced either secreted gp120 or full-length gp160. Mice immunized with gp120 DNA developed strong antigen-specific antibody responses, CD8+ cytotoxic T lymphocytes (CTL) (following in vitro restimulation with gp120-derived peptide), and showed in vitro proliferation and Th1-like cytokine secretion [gamma-interferon, interleukin (IL)-2 with little or no IL-4] by lymphocytes obtained from all lymphatic compartments tested (spleen, blood, and inguinal, iliac, and mesenteric lymph nodes). This indicated that systemic anti-gp120 cell-mediated immunity was induced by this DNA vaccine. Although similar antibody responses were observed in mice immunized by either intramuscular or intradermal routes, T cell responses were significantly stronger in mice injected intramuscularly. Rhesus monkeys immunized with both gp120 and gp160 DNAs exhibited significant CD8+ CTL responses, following in vitro restimulation of peripheral blood lymphocytes with antigen. These experiments demonstrate that DNA immunization elicits potent immune responses against HIV env in both a rodent and a nonhuman primate species.

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Intranasal immunization with a plant virus expressing a peptide from HIV-1 gp41 stimulates better mucosal and systemic HIV-1-specific IgA and IgG than oral immunization.

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Control of pandemic human immunodeficiency virus type 1 (HIV-1) infection ideally requires specific mucosal immunity to protect the genital regions through which transmission more often occurs. Thus a vaccine that stimulates a disseminated mucosal and systemic protective immune response would be extremely useful. Here we have investigated the ability of a chimeric plant virus, cowpea mosaic virus (CPMV), expressing a 22 amino acid peptide (residues 731-752) of the transmembrane gp41 protein of HIV-1 IIIB (CPMV-HIV/1), to stimulate HIV-1-specific and CPMV-specific mucosal and serum antibody following intranasal or oral immunization together with the widely used mucosal adjuvant, cholera toxin. CPMV-HIV/1 has been shown previously to stimulate HIV-1-specific serum antibody in mice by parenteral immunization. All mice immunized intranasally with two doses of 10 microg of CPMV-HIV/1 produced both HIV-1-specific IgA in faeces as well as higher levels of specific, predominantly IgG2a, serum antibody. Thus there was a predominantly T helper 1 cell response. All mice also responded strongly to CPMV epitopes. Oral immunization of the chimeric cowpea mosaic virus was less effective, even at doses of 500 microg or greater, and stimulated HIV-1-specific serum antibody in only a minority of mice, and no faecal HIV-1 specific IgA.

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